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(54) Title: GAMMA RADIATION STERILIZABLE MULTILAYER FILMS

(57) Abstract: Multilayer films comprising at least one external layer (A) selected from (i) ethylene-vinyl acetate copolymers (EVA) containing up to 10 % moles of units deriving from vinyl acetate or (ii) propylene copolymers containing up to 15 % moles of ethylene and/or α -olefins and at least one internal layer (B) comprising a polyolefin heterophase composition containing from 50 to 94 % by weight of a fraction which is insoluble in xylene at room temperature and from 6 to 50 % by weight of a fraction which is soluble in xylene at room temperature. These films show a high tolerance towards gamma radiations and can be used in the packaging of sterilizable medical articles.

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gamma radiation sterilizable multilayer films

The present invention relates to radiation resistant multilayer films useful in the packaging of sterilizable articles such as those used in the biomedical sector. In particular, the invention relates to multilayer films in which at least one internal layer (B) comprises a mixture of different propylene homo or copolymers and at least one external layer (A) at least a copolymer selected from ethylene copolymer or propylene copolymers.

A large use is made, in the biomedical sector, of propylene polymers for the preparation of medical devices such as syringes, that are to be radiation sterilized. Usually, these articles are sterilized with doses of 2.5 to 5 megarads of high-energy gamma radiation. It is known that at these doses the radiation-resistance of the polypropylene in itself is not sufficient to avoid the phenomena of embrittlement and discoloration after exposure to irradiation. The most used solution for this problem has been that of using various additives having the purpose of enhancing the polypropylene radiation resistance. Although these additives create some other problems like compatibility with other components, undesired odors, difficulties in processing etc., they actually mitigated the problem of the polypropylene radiation tolerance and, as mentioned above such a polymer, experienced a good success in the preparation of medical molded devices.

In spite of the use of additives, polypropylene confirmed to be an unsatisfactory material when extruded into sheets or films to be used in the packaging of the sterilizable articles. In the films in fact the ratio surface area/mass is very increased and, as a consequence, the radiation-resistance of the material becomes so lower that even the use of additives does not allow to obtain the required resistance in the film.

In addition, the use of certain additives in the polypropylene layer of the film can make said layer not much compatible with the external layers that, in turn, are required to show very good sealing properties in particular towards certain articles like medical papers.

It would be therefore important to have available a polypropylene based film having in itself a high tolerance towards gamma radiation and having at the same time good sealing properties. Very surprisingly, it has been found that multilayer films of a specific composition can meet the above requirements.

The multilayer films of the present invention are characterized in that at least one layer (A) thereof comprises (i) ethylene-vinyl acetate copolymers (EVA) containing up to 10% moles of units deriving from vinyl acetate or (ii) propylene copolymers containing up to 15% moles of

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ethylene and/or α -olefins $\text{CH}_2=\text{CHR}$, where R is an alkyl radical having from 2 to 10, and at least one layer (B) comprises a heterophasic polyolefin composition having:

- (a) from 50 to 94% by weight of a fraction which is insoluble in xylene at room temperature, comprising a propylene homopolymer or a copolymer of propylene with ethylene and/or another α -olefin $\text{CH}_2=\text{CHR}$, where R is an alkyl radical having 2-10 carbon atoms, this fraction containing more than 50% by weight of units derived from propylene; and
- (b) from 6 to 50% by weight of a fraction which is soluble in xylene at room temperature, comprising an amorphous copolymer of ethylene with propylene and/or another α -olefin $\text{CH}_2=\text{CHR}$, where R has the meaning described above, this fraction optionally containing smaller proportions of a diene and containing more than 15% by weight of units derived from ethylene; the percentages by weight of (a) and (b) being referred to the total weight of (a) + (b).

The α -olefin $\text{CH}_2=\text{CHR}$ may be selected, for example, from 1-butene, 1-hexene, 1-octene and 4-methyl-1-pentene; 1-butene is preferably used. The use of the component (i) in the layer (A) is especially preferred. The EVA copolymers used in the present invention are known in the art and commercially available. They are usually prepared by the free radical copolymerization process which can be carried out in the autoclave or in a tubular reactor. As mentioned above, the amount of vinyl acetate is lower than, or equal to, 10% by moles. However, EVA copolymers containing from 2.5 to 7% of vinyl acetate units are especially preferred. The Melt Index of said EVA copolymers is generally from 0.1 to 100, however, in the present invention, the use of EVA copolymers with Melt Index ranging from 0.5 to 5 is preferred.

The propylene copolymer (ii) that can be used in the layer (A) of the present invention are also known in the art. They can be prepared by copolymerization of propylene with ethylene or other α -olefin $\text{CH}_2=\text{CHR}$, in the presence of stereospecific Ziegler-Natta catalysts. These catalysts are obtained by reaction of an organometallic compound of a metal from groups II and III of the Periodic Table of the Elements with a catalytic component comprising a compound of a transition metal belonging to groups IV, V or VI of the Periodic Table of the Elements. For the preparation of the stereospecific copolymers used in the present invention the transition metal compound is preferably supported together with an electron donor compound (internal), on a magnesium halide in activated form. Moreover, another electron

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donor compound (external) is normally used together with the organometallic compound in order to increase the stereospecificity of the catalyst. Examples of catalysts which can be used in the preparation of the copolymer (i) are described for example in EP45977. Among the various propylene copolymers particularly preferred are the propylene copolymers with ethylene or butene-1 containing from 2 to 8% by mole of comonomer.

In the heterophasic composition present in the internal layer (B), the amount of the xylene insoluble fraction (a) ranges preferably from 60 to 90% of the total weight of (a) + (b). The amount of the xylene soluble fraction (b) ranges preferably from 10 to 40% of the total weight of (a) + (b).

The heterophasic polyolefin compositions used in layer (B) of the present invention can be directly obtained by mechanically blending the components (a) and (b) or, in alternative, such compositions can conveniently be prepared by sequential polymerization working in at least two stages; in a first stage, the crystalline propylene polymer is prepared, and, in a second stage, mixtures of ethylene, propylene and/or an α -olefin $\text{CH}_2=\text{CHR}$ are polymerized to give a predominantly amorphous copolymer.

These heterophasic compositions can conveniently be prepared using a highly stereospecific catalyst, of the type described in the patent application EP-A-395,083. Examples of heterophasic compositions and methods for preparing them are described in USP 4,521,566, EP-A-400,333 and EP-A-472,946. The polymerization is conveniently carried out in the gas phase using fluidized-bed reactors. Examples of products prepared according to this method are described in patent applications WO 93/03078 and WO95/20009.

The fraction (a) which is insoluble in xylene can, in its turn, be constituted by a combination of components. In a preferred aspect of the invention, the xylene insoluble fraction (a1) is constituted by a combination of an isotactic propylene homopolymer, a propylene copolymer with butene-1 containing from 4 to 10% of butene-1 units and a crystalline copolymer of ethylene with butene-1 having less than 15% by weight of butene-1. These three components are blended in ratio such as to give the resulting fraction (a) containing at least 50% by weight of propylene units. When the xylene insoluble fraction (a1) is used its amount on the total weight of (a) + (b) ranges preferably from 75 to 90%.

The fraction (b) which is soluble in xylene is preferably an amorphous copolymer of ethylene with propylene or butene-1. Preferably, it is a soluble fraction (b1) containing a copolymer of ethylene with butene-1 having more than 15% by weight of butene-1 units. In this case the

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amount of fraction (b1) ranges preferably from 10 to 25% by weight based on the total of (a) + (b).

Practically, the preferred heterophasic compositions (a1)+(b1) used in the internal layer (B) of the present invention can be obtained by mechanically blending an amorphous or crystalline component with an heterophasic composition comprising a crystalline and an amorphous fraction and obtained by the sequential polymerization process described above. For example the final heterophasic compositions can be obtained by blending the propylene/ butene-1 copolymer containing from 4 to 10% of butene-1 units with a heterophasic composition comprising a xylene insoluble fraction composed of the isotactic propylene homopolymer and of the crystalline copolymer of ethylene with butene-1 having less than 15% by weight of butene-1 and a xylene soluble fraction composed of a copolymer of ethylene with butene-1 having more than 15% by weight of butene-1 units.

The mechanical blend can be made before feeding the final heterophasic composition to the extruder by mixing the two components in the molten state in a mixer with mixing efficiency.

The multilayer films according to the present invention are preferably prepared by the known technology of film extrusion through a flat head. In particular, in the case of the present multilayer films, two or more parallel extruders, fed with the desired polyolefin compositions, convey the molten material to a flat collecting head provided with a slot from which the superimposed molten layers emerge. The said layers are then extruded onto a rotating cylinder with a cooling facility (chill roll) which allows solidification of the extrudate with formation of the polymer film. The layer in contact with the chill roll is termed "lower outer layer". The spin speed of the chill roll can be adjusted so as to provide films of the desired thickness.

In general, the thickness of the films ranges from 30 to 150 μm , preferably from 40 to 120 μm and more preferably from 50 to 110 μm .

The films obtained by the process described above may also have layers additional to the layers (A) and (B) described above. The said additional layers may be identical in composition to the layer (A) or the layer (B), or alternatively they may be different from either (A) or (B).

A particularly preferred aspect of the present invention relates to films consisting of three layers, with a structure of the type ABA, in which between the two outer layers A is placed an intermediate layer B as defined above. The weight ratio between the external layers (A) and the internal layer (B) can vary. Generally, the weight ratio between the internal layer and one of the external layers is between 20:1 and 1:5, preferably between 10:1 and 1:2.

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It is a preferred embodiment of the present invention a gamma radiation sterilizable film of the ABA structure in which both the outer layers (A) comprise the component (i) while the inner layer (B) comprises the fractions the fractions (a1), and (b1) as defined above.

The various layers (A) and (B) can be present in variable amounts relative to the total weight of the film. Preferably, each of the two outer layers is present in amounts generally ranging from about 5 to about 45% relative to the total weight of the film. More preferably, each outer layer is present in amounts of between 10 and 30%. The two outer layers are preferably present in equal parts.

According to what has been mentioned above, the films of the present invention are characterized, after the sterilizing gamma radiation treatment, by excellent mechanical properties in terms of tear strength, and elongation at break, and in particular by an excellent impact resistance.

The weight ranges described for the components present in the layers of the films of the present invention refer to the relative weight ratios of the components (i), (ii), (a), and (b) [or (a1) and (b1)]. Obviously, in accordance with what is known by those skilled in the art further polymeric components, additives (such as, for example, adhesives, stabilizers, antioxidants, anti-corrosion agents, etc.) and fillers, of either organic or inorganic nature, that are capable of imparting specific properties to the films of the invention may be added. Residues obtained by trimming the films produced may also be among the various components which may be added. The said residues are generally reintroduced in the central extruder.

The examples which follow are given by way of illustration of the invention, without any limitation thereof being implied.

EXAMPLES

CHARACTERIZATION

The properties indicated were determined according to the following methods:

- Composition of the polymers: weight percentage of the various monomers determined by I.R.;
- Insolubility in xylene: 2g of polymer are dissolved in 250cm³ of xylene at 135°C with stirring. After 20 minutes the solution is left to cool with continued stirring until it reaches a temperature of 25°C. After 30 minutes the insoluble polymer precipitated is separated out by filtration. The solvent is removed from the solution by evaporation under a stream of nitrogen and the residue is dried under vacuum at 80°C until the

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weight remains constant. In this way, the percentage of polymer soluble in xylene at 25°C is calculated and, consequently, the percentage of insoluble polymer is determined;

- Melt Index E (MIE): ASTM D 1238, condition E;
- Melt Index L (MIL): ASTM D 1238, condition L;
- Elmendorf Tear Strength: ASTM D 1922, determined both in the direction of the machine (MD) and in the transverse direction (TD);
- Elongation at break: ASTM D 882
- Impact resistance (Dart test): ASTM D 1709
- Coefficient Of Friction (COF): ASTM D1894

EXAMPLE 1

A multilayer film of the ABA structure with a total thickness of about 90µm was prepared according to the method of coextrusion through a flat head described above, using a Reifenhauser film line fitted with two extruders for the outer layers (diameter 70mm) and a extruder for the inner layer (diameter 100mm). The thickness of the internal layer was 50µm while the thickness of the outer layers was 20 µm each. Both the outer layers were composed of a EVA copolymer marketed by EXXON under the name Escorene LD362 BR containing 4.5% of vinyl acetate units and with a MIE of 2. The layer (B) was composed of a final heterophasic composition comprising 87.5% of a xylene insoluble fraction and 12.5% of a xylene soluble fraction said final composition being obtained by mechanical blending a propylene random copolymer containing 8%by weight of butene-1 and having a Melt Index of 9, with an equal weight of a first heterophasic composition comprising 30% of a propylene homopolymer, 45% of a ethylene-butene-1 crystalline copolymer containing less than 15% of butene-1 units and 25% of an amorphous ethylene-butene-1 copolymer containing more than 15% of butene-1 units; said first heterophasic composition having a total amount of ethylene of 57%, a total amount of butene-1 of 11% and a Melt Index of 7.

The so obtained film has been exposed to cobalt 60 gamma radiation at a dose level of 3.5Mrad using conventional techniques and apparatus. The results of the characterization test are reported in Table 1.

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TABLE 1

Property	Meas. unit	Method	Value
Tensile Module MD	psi	ASTM D882	4530
Tensile Module TD	"	ASTM D882	4020
Elong. at break, MD	%	ASTM D882	588
Elong. at break TD	"	ASTM D882	790
Tear Strength MD	grams	ASTM D1922	596
Tear Strength TD	"	ASTM D1922	1451
Impact resist. (dart test)	"	ASTM D1709	467
C.O.F seal layer		ASTM D1894	0,15

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CLAIMS

1. Gamma radiation sterilizable multilayer films characterized in that at least one layer (A) thereof comprises (i) ethylene-vinyl acetate copolymers (EVA) containing up to 10% moles of units deriving from vinyl acetate or (ii) propylene copolymers containing up to 15% moles of ethylene and/or α -olefins $\text{CH}_2=\text{CHR}$, where R is an alkyl radical having from 2 to 10, and at least one layer (B) comprises a heterophasic polyolefin composition having:
 - (a) from 50 to 94% by weight of a fraction which is insoluble in xylene at room temperature, comprising a propylene homopolymer or a copolymer of propylene with ethylene and/or another α -olefin $\text{CH}_2=\text{CHR}$, where R is an alkyl radical having 2-10 carbon atoms, this fraction containing more than 50% by weight of units derived from propylene; and
 - (b) from 6 to 50% by weight of a fraction which is soluble in xylene at room temperature, comprising an amorphous copolymer of ethylene with propylene and/or another α -olefin $\text{CH}_2=\text{CHR}$, where R has the meaning described above, this fraction optionally containing smaller proportions of a diene and containing more than 15% by weight of units derived from ethylene; the percentages by weight of (a) and (b) being referred to the total weight of (a) + (b).
2. Multilayer films according to Claim 1, in which the layer (A) is composed of the component (I).
3. Multilayer films according to Claim 2, in which the EVA copolymer contains from 2.5 to 7% of vinyl acetate units.
4. Multilayer films according to one or more of the preceding claims, in which in the heterophasic composition present in the internal layer (B) the amount of the xylene insoluble fraction (a) ranges from 60 to 90% and the amount of the xylene soluble fraction (b) ranges from 10 to 40% of the total weight of (a) + (b).
5. Multilayer films according to claim 2 in which the layer (B) comprises a xylene insoluble fraction (a1) comprising an isotactic propylene homopolymer, a propylene copolymer with butene-1 containing from 4 to 10% of butene-1 units and a crystalline copolymer of ethylene with butene-1 having less than 15% by weight of butene-1 and a xylene soluble fraction (b1) containing a copolymer of ethylene with butene-1 having more than 15% by weight of butene-1 units.

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6. Multilayer films according to claim 5 in which the amount of the xylene insoluble fraction (a1) is from 75 to 90% of the total weight of (a1) + (b1) and the amount of the fraction (b1) is from 10 to 25% by weight based on the total of (a1) + (b1).
7. Multilayer films according to claim 6 in which the heterophasic composition (a1)+(b1) is obtained by blending a propylene/butene-1 copolymer, containing from 4 to 10% of butene-1 units, with a heterophasic composition comprising a xylene insoluble fraction comprising from 20 to 40% of isotactic propylene homopolymer from 30 to 60% of a crystalline copolymer of ethylene with butene-1 having less than 15% by weight of butene-1 and from 10 to 50% of a xylene soluble fraction composed of a copolymer of ethylene with butene-1 having more than 15% by weight of butene-1 units.
8. A gamma radiation sterilizable film of the ABA structure in which both the outer layers (A) comprise the component (i) while the inner layer (B) comprises the fractions (a1) and (b1) as defined above.
9. Use of the films according to claims 1-8 in the packaging of gamma radiation sterilizable biomedical articles.

INTERNATIONAL SEARCH REPORT

Int. Appl. No.
PCT/EP 01/01209A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C08L23/10 B32B27/32

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C08L B32B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 140 073 A (ROLANDO RICHARD J ET AL) 18 August 1992 (1992-08-18)	1,8,9
Y	column 11, line 33 -column 12, line 20-26; claims 1-4; figures 6-8-11; examples 23A-25D; tables V-VI	2
Y	WO 98 54251 A (COLLINA GIANNI ;PELLICONI ANTEO (IT); MONTELL NORTH AMERICA INC. (U) 3 December 1998 (1998-12-03) claims 1,2,5	1,4-9
X	US 4 857 409 A (HAZELTON DONALD R ET AL) 15 August 1989 (1989-08-15)	1,4,8,9
Y		2,4-7
X	column 3, line 8-23; claims 1-4,6-8,10,13,15-17,22,23,29	5

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

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L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another claim or other special reason (as specified)

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X document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

Z document member of the same patent family

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 863 183 A (CHISSO CORP) 9 September 1998 (1998-09-09) page 9-11-14 -page 43-44; claims 1-5,11,20-23,25-27	1,4,6
X	page 10, line 47 -page 11, line 1-6-30; claims 20,27	2,3
A	page 42, line 38; tables 11,12	7
P,X	WO 00 11079 A (CHISSO CORP ;HIROSE TAKETO (JP); AKITAYA SINICHI (JP); HATTORI TAK) 2 March 2000 (2000-03-02) the whole document	1,9
P,X	DE 199 15 314 A (ALKOR GMBH) 5 October 2000 (2000-10-05) claims 1,10-13,17	1
P,Y	EP 1 066 958 A (CRYOVAC INC) 10 January 2001 (2001-01-10) claims 1-11	1

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Information on patent family members

Int. :ional Application No

PCT/EP 01/01209

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5140073 A	18-08-1992	AU 623997 B	28-05-1992
		AU 5580590 A	03-01-1991
		DE 69011230 D	08-09-1994
		DE 69011230 T	26-01-1995
		EP 0405793 A	02-01-1991
		IE 901796 A	02-01-1991
		JP 3039341 A	20-02-1991
		US 5258419 A	02-11-1993
		US 5209984 A	11-05-1993
WO 9854251 A	03-12-1998	IT MI971258 A	30-11-1998
		EP 0918821 A	02-06-1999
		JP 2000515582 T	21-11-2000
		US 6180720 B	30-01-2001
US 4857409 A	15-08-1989	AU 591062 B	30-11-1989
		AU 4371385 A	19-12-1985
		CA 1264517 A	23-01-1990
		DE 3579758 D	25-10-1990
		EP 0165791 A	27-12-1985
EP 0863183 A	09-09-1998	AU 7638796 A	11-06-1997
		BR 9611825 A	13-07-1999
		WO 9719135 A	29-05-1997
WO 0011079 A	02-03-2000	NONE	
DE 19915314 A	05-10-2000	NONE	
EP 1066958 A	10-01-2001	NONE	

Form PCT/ISA/210 (patent family annex) (July 1992)